CLAIMS

What is claimed is:

1. A method for forming a polymerized hemoglobin solution, comprising contacting a stabilized hemoglobin solution with a polymerizing agent, said stabilized hemoglobin solution including tetrameric and polymeric hemoglobin, whereby at least a portion of the hemoglobin solution is further polymerized, thereby producing the polymerized hemoglobin solution.

2. A method of Claim 1, wherein the stabilized hemoglobin is present in a physiological buffer when contacted with the polymerizing agent.

3. A method of Claim 2, wherein the physiological buffer has a pH of about 7.6 to about 7.9.

4. A method of Claim 2, wherein the physiological buffer includes at least one component selected from the group consisting of: sodium lactate, N-acetyl-L-cysteine, sodium chloride, potassium chloride, and calcium chloride•$2H_2O$.

5. A method of Claim 3, wherein the physiological buffer includes sodium lactate at a concentration of about 290 to about 330 mg/100 ml.

6. A method of Claim 3, wherein the physiological buffer includes N-acetyl-L-cysteine at a concentration of about 130 to about 220 mg/100 ml.

7. A method of Claim 3, wherein the physiological buffer includes sodium chloride at a concentration of about 570 to about 620 mg/100 ml.

8. A method of Claim 3, wherein the physiological buffer includes potassium chloride at a concentration of about 27 to about 33 mg/100 ml.

9. A method of Claim 3, wherein the physiological buffer includes calcium chloride•$2H_2O$ at a concentration of about 18 to about 22 mg/100 ml.

10. A method of Claim 1, wherein the stabilized hemoglobin solution comprises bovine hemoglobin.

11. A method of Claim 1, wherein the concentration of the hemoglobin in the stabilized hemoglobin solution during the further polymerization is about 40 grams per liter.

12. The method of Claim 1, further including the step of forming the stabilized hemoglobin solution by contacting native hemoglobin with a cross-linking and/or polymerizing agent.

13. The method of Claim 12, wherein forming the stabilized hemoglobin solution includes directing a solution of polymerized, native hemoglobin through a filter having a molecular weight cut off of at least about 100 kD, whereby resulting filtrate is the stabilized hemoglobin solution.

14. A method of Claim 13, wherein the polymerizing agent is glutaraldehyde.

15. A method of Claim 1, wherein the concentration of glutaraldehyde added to the stabilized hemoglobin solution is about 1 to about 20 grams of glutaraldehyde per kilogram of total hemoglobin present in the stabilized hemoglobin solution.

16. A method of Claim 15, wherein the concentration of glutaraldehyde in the stabilized hemoglobin solution is about 10 grams of glutaraldehyde per kilogram of total hemoglobin present in the stabilized hemoglobin solution.

17. A method of Claim 1, wherein no more than about 10% by weight of the hemoglobin present in the polymerized hemoglobin solution has a molecular weight of at least about 500 kD.

18. A method of Claim 1, wherein between about 45% and about 65% by weight of total hemoglobin present in the polymerized hemoglobin solution is tetrameric and octameric hemoglobin.

19. A method of Claim 1, wherein no more than about 40% by weight of total hemoglobin present in the polymerized hemoglobin solution has as molecular weight of about 65 kD or less.

20. A method of Claim 1, wherein no more than 10% by weight of total hemoglobin present in the polymerized hemoglobin solution is methemoglobin.

21. The method of Claim 1, further comprising directing the polymerized hemoglobin through a filter having a molecular weight cut off of at least about 100 kD, whereby the resulting retentate comprises a polymerized hemoglobin, wherein no more than about 15% by weight of the hemoglobin present in the retentate has a molecular weight of at least about 500 kD, and no more than about 10% by weight of the hemoglobin present in the retentate has a molecular weight of about 65 kD or less.

22. A method for forming a polymerized hemoglobin solution, comprising contacting a stabilized hemoglobin solution with glutaraldehyde at a

concentration of about 1 to about 20 grams of glutaraldehyde per kilogram of hemoglobin present in the stabilized hemoglobin solution, said stabilized hemoglobin solution including a physiological buffer, whereby at least a portion of the hemoglobin is polymerized, thereby forming the polymerized hemoglobin solution.

23. A method of Claim 22, wherein the physiological buffer has a pH of about 7.6 to about 7.9.

24. A method of Claim 22, wherein the physiological buffer includes at least one component selected from the group consisting of: sodium lactate, N-acetyl-L-cysteine, sodium chloride, potassium chloride, and calcium chloride•$2H_2O$.

25. A method of Claim 22, wherein the physiological buffer includes sodium lactate at a concentration of about 290 to about 330 mg/100 ml.

26. A method of Claim 22, wherein the physiological buffer includes N-acetyl-L-cysteine at a concentration of about 130 to about 220 mg/100 ml.

27. A method of Claim 22, wherein the physiological buffer includes sodium chloride at a concentration of about 570 to about 620 mg/100 ml.

28. A method of Claim 22, wherein the physiological buffer includes potassium chloride at a concentration of about 27 to about 33 mg/100 ml.

29. A method of Claim 22, wherein the physiological buffer includes calcium chloride•$2H_2O$ at a concentration of about 18 to about 22 mg/100 ml.

30. A method of Claim 22, wherein the stabilized hemoglobin solution comprises bovine hemoglobin.

31. A method of Claim 22, wherein the concentration of the hemoglobin in the stabilized hemoglobin solution during the further polymerization is about 40 grams per liter.

32. The method of Claim 22, further includes the step of forming the stabilized hemoglobin solution.

33. The method of Claim 22, further including the step of forming the stabilized hemoglobin solution by contacting native hemoglobin with either or both of a cross-linking and polymerizing agent, resulting in polymerized, native hemoglobin.

34. The method of Claim 33, wherein forming the stabilized hemoglobin solution includes directing a solution of polymerized, native hemoglobin through a filter having a molecular weight cut off of at least about 100 kD, whereby resulting filtrate is the stabilized hemoglobin solution.

35. A method of Claim 22, wherein the concentration of glutaraldehyde added to the stabilized hemoglobin solution is about 10 grams of glutaraldehyde per kilogram of total hemoglobin present in the stabilized hemoglobin solution.

36. A method of Claim 22, wherein no more than about 10% by weight of the hemoglobin present in the polymerized hemoglobin solution has a molecular weight of greater than about 500 kD.

37. A method of Claim 22, wherein between about 45% and about 65% by weight of total hemoglobin present in the polymerized hemoglobin solution is tetrameric and octameric hemoglobin.

38. A method of Claim 22, wherein no more than about 40% by weight of total hemoglobin present in the polymerized hemoglobin solution has a molecular weight of about 65 kDa or less.

39. A method for forming a polymerized hemoglobin solution, comprising contacting a stabilized hemoglobin solution with glutaraldehyde at a concentration of about 1 to about 20 grams of glutaraldehyde per kilogram of hemoglobin present in the stabilized hemoglobin solution, said stabilized hemoglobin solution including hemoglobin tetramers, wherein the stabilized hemoglobin solution includes N-acetyl-L-cysteine at a concentration of about 130 to about 220 mg/100 ml, sodium lactate at a concentration of about 290 to about 330 mg/100 ml, sodium chloride at a concentration of about 570 to about 620 mg/100 ml, potassium chloride at a concentration of about 27 to about 33 mg/100 ml, calcium chloride•$2H_2O$ at a concentration of about 18 to about 22 mg/ 100 ml and having a pH of about 7.6 to about 7.9, whereby at least a portion of the hemoglobin is polymerized, thereby forming a polymerized hemoglobin solution wherein no more than about 10% by weight of total hemoglobin present in the hemoglobin solution has a molecular weight of at least about 500 kDa, no more than about 40% by weight of total hemoglobin has a molecular weight of about 65 kD or less, and no more than about 10% by weight of total hemoglobin is methemoglobin.

40. A method of Claim 39, wherein the stabilized hemoglobin solution comprises bovine hemoglobin.

41. A method of Claim 39, wherein the concentration of the hemoglobin in the stabilized hemoglobin solution during the further polymerization is about 40 grams per liter.

42. The method of Claim 39, further including the step of forming the stabilized hemoglobin solution by contacting native hemoglobin with a cross-linking and/or polymerizing agent, resulting in polymerized, native hemoglobin.

43. The method of Claim 42, wherein forming the stabilized hemoglobin solution includes directing a solution of polymerized, native hemoglobin through a filter having a molecular weight cut off of at least about 100 kD, whereby resulting filtrate is the stabilized hemoglobin solution.

44. A method for forming a polymerized hemoglobin solution, comprising:

a) contacting a stabilized hemoglobin solution with glutaraldehyde at a concentration of about 1 to about 20 grams of glutaraldehyde per kilogram of hemoglobin present in the stabilized hemoglobin solution, said stabilized hemoglobin solution including hemoglobin tetramers, wherein the stabilized hemoglobin solution includes N-acetyl-L-cysteine at a concentration of about 130 to about 220 mg/100 ml, sodium lactate at a concentration of about 290 to about 330 mg/100 ml, sodium chloride at a concentration of about 570 to about 620 mg/100 ml, potassium chloride at a concentration of about 27 to about 33 mg/100 ml, calcium chloride•$2H_2O$ at a concentration of about 18 to about 22 mg/ 100 ml and having a pH of about 7.6 to about 7.9, whereby at least a portion of the hemoglobin is polymerized; and

b) directing the polymerized hemoglobin of a) through a filter having a molecular weight cut off of at least about 100 kD, and obtaining the retentate;

thereby forming a polymerized hemoglobin solution, wherein no more than about 15% by weight of the hemoglobin present in the retentate has a molecular weight of at least about 500 kD, and no more than about 10% by weight of the hemoglobin present in the retentate has a molecular weight of about 65 kD or less.